CLAIMS

What is claimed is:

1. A method for identifying a compound as a non-competitive inhibitor of a ligand-gated neurotransmitter ion channel receptor comprising:

i) determining the log k' for binding of the compound to the ligand-gated neurotransmitter ion channel receptor, or to a subunit thereof;

ii) determining the energy of the highest occupied molecular orbital of the compound in eV;

iii) determining the area in $Å^2$ of a plane projection of the compound; and

iv) identifying as an effective non-competitive inhibitor a compound exhibiting all of log k' from 1.1 to 1.9, an energy of the highest occupied molecular orbital from –8.6 to –9.2 eV and a YZ shadow of 25 to 50 $Å^2$.

2. A method for making a pharmaceuctical composition comprising admixing a compound identified by the method of claim 1 with a pharmaceutically acceptable carrier.

3. The method of claim 1, in which k' is determined using docking of a computational model of the compound to a computational model of the luminal channel of the ligand-gated neurotransmitter ion channel receptor.

4. The method of claim 1, in which k' is determined by chromatography of the compound on an affinity matrix comprising at least one subunit polypeptide of the ligand-gated neurotransmitter ion channel receptor.

5. The method of claim 1, in which the ligand-gated neurotransmitter receptor has a subunit stoichiometry ranging from $(\alpha)_5(\beta)_0$ to $(\alpha)_2(\beta)_3$, or $(\alpha)_2\beta\delta\gamma$.

6. The method of claim 5, in which the stoichiometry is $(\alpha)_2(\beta)_3$.

7. The method of claim 6, in which the model of the luminal channel of the ligand-gated neurotransmitter ion channel receptor has the atomic coordinates of the α3β4 subtype receptor or the α3β2 subtype receptor shown in Appendix 4 or Appendix 5, respectively.

8. A compound that is a derivative of dextromethorphan having the nitrogen-bound methyl group substituted by a C_{1-6} alkyl group bearing a hydrogen-bond accepting group.

9. The compound of claim 8, in which the hydrogen bond accepting group is a keto group, a guanidinium group or a nitrogen-containing heterocyclic group.

10. The compound of claim 9, in which the nitrogen-containing heterocyclic group is a pyrollidine, imidazolidine, piperidine, hexahydropyrimidine or pyrimidine group.

11. A compound comprising

a hydrophobic group comprising a saturated or unsaturated alkyl chain containing 4 to 10 carbon atoms, a saturated hydrocarbon ring containing 5 or 6 carbon atoms, or at least one ring that includes at least two conjugated unsaturated bonds, said ring optionally being fused to additional rings to form a ring system and said additional rings optionally including one or more hetero atoms;

a hydrogen bond accepting group selected from the group consisting of a keto group, a nitrogen-containing heterocyclic group and a guanidinium group;

a linker joining said hydrophobic group and said hydrogen bond accepting group and comprising 1 to 4 carbon atoms and optionally containing an oxygen or sulfur atom;

the compound having activity as a non-competitive inhibitor of Rb^+ efflux of a ligand-gated neurotransmitter ion channel receptor with an IC_{50} of less than 10 μM.

12. The compound of claim 11, in which the ring is a planar, aromatic ring system.

13. The compound of claim 11, in which the ring is selected from the group consisting of a phenyl ring, a napthyl ring, morphinan and dibenzo [1.4] diazepine.

14. A computer system comprising:

i) a memory storing positional data of the atomic coordinates of the transmembrane portion of at least one subunit of a ligand-gated neurotransmitter receptor protein; and

ii) a processor generating a molecular model having a three dimensional shape representative of a luminal domain portion of the ligand-gated neurotransmitter receptor having a stochiometry of $(\alpha)_2(\beta)_3$ based the positional data.

15. The computer system of claim 14, in which the α subunits are α3 subtype and the β subunits are β2 or β4 subtype.

16. A method for treating Tourette's syndrome, schizophrenia, a cognitive disorder, pain, anxiety, depression, neurodegeneration or an

addiction caused by an overactive ligand-gated ion channel receptor, comprising administering to a subject an amount of a compound of claim 11 effective to inhibit ion flux through said ligand-gated ion channel.